

We claim:

1. A method for delivering a DNA to a mammal, said DNA encoding a peptide or protein operably linked to a promoter, the method comprising exposing said mammal to a composition comprising an ionizable or ionized transition metal enhancer and said DNA,  
5 wherein said DNA expresses said peptide or protein.

2. The method of Claim 1, wherein said DNA is expressed in a secretory gland of said mammal.

10 3. The method of Claim 2, wherein the secretory gland is selected from the group consisting of a salivary gland, a pancreas, a mammary gland, a thyroid, a thymus, a pituitary gland, and a liver.

15 4. The method of Claim 3, wherein the secretory gland is a salivary gland or a pancreas.

5. The method of Claim 2, wherein said peptide or protein is secreted or released from said secretory gland.

20 6. The method of Claim 2, wherein the peptide or protein is not secreted from the secretory gland.

25 7. The method of Claim 1, wherein said DNA is expressed in the lung, muscle, brain, blood, breast, bone, bladder, skin, liver, stomach, intestine, kidney, testes, uterus, testes, uterus, gastrointestinal tract, or ovaries of said mammal.

8. The method of Claim 7, wherein said DNA is expressed in the lung, muscle, or brain of said mammal.

30 9. The method of Claim 8, wherein said DNA is expressed in the lung of said mammal.

10. The method of Claim 1, wherein said composition is delivered to said mammal by a route of administration selected from the group consisting of intramuscular, intratracheal, intraperitoneal, intradermal, intravenous, intraperineal, subcutaneous, sublingual, intranasal inhalation, intranasal instillation, intrarectal, intravaginal, ocular, oral, intraductal, and topical administration.

11. The method of Claim 1, wherein the composition is a solution having a pH of about 4.0 to about 9.0.

12. The method of Claim 11, wherein the composition is a solution having a pH of about 5.5 to about 8.5.

13. The method of Claim 1, wherein the composition is a solution having a total salt concentration of less than about 250 micromolar.

14. The method of Claim 1, wherein the composition is a solution having a cumulative salt concentration of less than about 50 micromolar.

15. The method of Claim 1, wherein said mammal is exposed to about 1 microgram to about 100 milligrams of the DNA.

16. The method of Claim 1, wherein said mammal is exposed to about 30 micrograms to about 30 milligrams of the DNA.

17. The method of Claim 1, wherein a molar ratio of the ionizable or ionized transition metal enhancer to DNA in the composition is about 0.0001:1 to about 1:0.0001.

18. The method of Claim 1, wherein the ionizable or ionized transition metal enhancer is a complex, adduct, cluster or salt of an element selected from the group consisting of a *d*-block element, a first row *f*-block element, aluminum, and gallium.

19. The method of Claim 18, wherein the ionizable or ionized transition metal enhancer is a complex, adduct, cluster or salt of an element selected from the group consisting of zinc, nickel, cobalt, copper, aluminum, and gallium.

5           20. The method of Claim 19, wherein the ionizable or ionized transition metal enhancer is selected from the group consisting of zinc sulfate, zinc acetate, nickel sulfate, nickel acetate, cobalt sulfate, cobalt acetate, copper sulfate, and copper acetate.

10           21. The method of Claim 20, wherein the ionizable or ionized transition metal enhancer is zinc acetate or zinc sulfate.

          22. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{ZnCl}_2$  to about 250 millimolar  $\text{ZnCl}_2$  in said solution.

15           23. The method of Claim 22, wherein the ionizable or ionized transition metal enhancer is about 0.03 millimolar zinc sulfate to about 6.0 millimolar zinc sulfate in said solution.

20           24. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar zinc acetate to about 250 millimolar zinc acetate in said solution.

25           25. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.03 millimolar zinc acetate to about 6.0 millimolar zinc acetate in said solution.

30           26. The method of Claim 1, wherein the ionizable or ionized transition metal enhancer is selected from the group consisting of zinc halide, nickel halide, cobalt halide, copper halide, aluminum halide, and gallium halide.

27. The method of Claim 26, wherein the ionizable or ionized transition metal enhancer is selected from the group consisting of  $\text{ZnCl}_2$ ,  $\text{NiCl}_2$ ,  $\text{CoCl}_2$ ,  $\text{CuCl}_2$ ,  $\text{AlCl}_3$ , and  $\text{GaCl}_3$ .

5            28. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{ZnCl}_2$  to about 250 millimolar  $\text{ZnCl}_2$  in said solution.

10           29. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.03 millimolar  $\text{ZnCl}_2$  to about 6.0 millimolar  $\text{ZnCl}_2$  in said solution.

15           30. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{NiCl}_2$  to about 250 millimolar  $\text{NiCl}_2$  in said solution.

            31. The method of Claim 30, wherein the ionizable or ionized transition metal enhancer is about 0.03 millimolar  $\text{NiCl}_2$  to about 6.0 millimolar  $\text{NiCl}_2$  in said solution.

20           32. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{CoCl}_2$  to about 250 millimolar  $\text{CoCl}_2$  in said solution.

25           33. The method of Claim 32, the ionizable or ionized transition metal enhancer is about 0.03 millimolar  $\text{CoCl}_2$  to about 6.0 millimolar  $\text{CoCl}_2$  in said solution.

30           34. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{CuCl}_2$  to about 250 millimolar  $\text{CuCl}_2$  in said solution.

35. The method of Claim 34, wherein the ionizable or ionized transition metal enhancer is about 0.03 millimolar  $\text{CuCl}_2$  to about 6.0 millimolar  $\text{CuCl}_2$  in said solution.

36. The method of Claim 1, wherein the composition is a solution and the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{AlCl}_3$  to about 250 millimolar  $\text{AlCl}_3$  in said solution.

37. The method of Claim 36, wherein the ionizable or ionized transition metal enhancer is about 0.01 millimolar  $\text{AlCl}_3$  to about 250 millimolar  $\text{AlCl}_3$  in said solution.

38. The method of Claim 1, wherein the DNA is a plasmid.

39. The method of Claim 1, wherein said protein is selected from the group consisting of insulin, human growth hormone, erythropoietin, clotting factor VII, bovine growth hormone, platelet derived growth factor, clotting factor VIII, thrombopoietin, interleukin-1, interleukin-2, interleukin-1 RA, superoxide dismutase, catalase, fibroblast growth factor, neurite growth factor, granulocyte colony stimulating factor, L-asparaginase, uricase, chymotrypsin, carboxypeptidase, sucrase, calcitonin, Ob gene product, glucagon, transforming growth factor, ciliary neurite transforming factor, insulin-like growth factor-1, granulocyte macrophage colony stimulating factor, interferon  $\alpha 2A$ , brain-derived neurite factor, insulintropin, tissue plasminogen activator, urokinase, streptokinase, adenosine deamidase, calcitonin, arginase, phenylalanine ammonia lyase,  $\gamma$ -interferon, pepsin, trypsin, elastase, lactase, intrinsic factor, cholecystokinin, insulinotrophic hormone clotting factor I, glucagon-like protein-I,  $\alpha$ -1-antitrypsin, glucocerebrosidase, cystic fibrosis transreductase, angiostatin, endostatin, angiogenics, and antiangiogenics.

40. A method of delivering a DNA into a mammalian pancreas, liver, salivary gland or mouse lung, said DNA encoding a peptide or protein operably linked to a promoter, the method comprising exposing said mammal to a composition comprising said DNA and an ionizable or ionized transition metal enhancer selected from the group consisting of zinc

chloride, copper chloride, nickel chloride, cobalt chloride, zinc sulfate, and zinc acetate, wherein said DNA is expressed.

5           41. A method for delivering a DNA to a cell of a mammal, said DNA encoding a peptide or protein operably linked to a promoter, the method comprising administering into said cell of said mammal a composition comprising an ionizable or ionized transition metal enhancer and said DNA.

10           42. The method of claim 1, said composition further comprising an a cationic lipid.

          43. The method of claim 42, wherein a cationic lipid:DNA phosphate ratio of said composition is about 0.01 to about 12.

15           44. The method of claim 42, wherein said cationic lipid is selected from the group consisting of 1:1 N,N-[bis(2-hydroxyethyl)]-N-methyl-N-[2,3-bis(tetradecanoyloxy)propyl]ammonium chloride and N,N,N',N'-tetramethyl-N,N'-bis(2-hydroxyethyl)-2,3-bis(9(z)-octadecenoyloxy)-1,4-butanediaminium iodide.